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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/705,286	11/02/2000	Weihong Xiong	T8341.NP	4704

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EXAMINER	
GHALI, ISIS A D	
ART UNIT	**PAPER NUMBER**
1615	9

DATE MAILED: 06/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/705,286	Applicant(s) XIONG ET AL.	
	Examiner Isis Ghali	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-52* is/are pending in the application.

4a) Of the above claim(s) *29-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The receipt is acknowledged of applicants' amendment A, filed03/24/2003.

Claims 1-28 are included in the prosecution.

1. This application contains claims 29-52 drawn to nonelected invention and species, nonelected without traverse in Paper No. 6. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

The standing rejections:

Claim Rejections - 35 USC § 103

2. Claims 1-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of US 6,352,715 ('715), US 6,159,986 ('986) or CN 1111987 ('987).

US '715 teaches a transdermal drug delivery system to administer huperzine A in a controlled release skin patch designed for once-a-week application. The device comprises a solvent to form a reservoir or it may contain a pressure sensitive adhesive polymer (abstract; col.3, lines 55-65; col.4, lines 7-15; col.9, lines 1-7, 31). The reference teaches a combination of co solvents to increase the skin permeation of huperzine (col.8, lines 65-67).

US '986 teaches a therapies and compounds for the inhibition of memory loss comprising transdermal administration of huperzine A in combination with plant extract, antioxidants, herbs (e.g. ginkgo, ginseng, Echinacea), amino acids, vitamins, and delivery enhancer (abstract; col.2, lines 6-20, 62; col.3, lines 8-18).

CN '987 teaches a plaster for treating senile dementia with long activity life of 3-4 days comprising huperzine and permeation enhancer (abstract).

The references do not teach the specific permeation enhancers claimed by applicants, the blood plasma levels, or the estrogen in combination with huperzine.

Fatty acids, fatty acid esters, fatty alcohols, surfactants, terpenes, and pyrrolidone derivatives are all known in the art as permeation enhancer, and are widely used in the transdermal art.

It is within the skill in the art to adjust the amount of the drug in order to achieve a therapeutic blood level for a predetermined period.

Transdermal delivery of combination of drugs is known and widely used in the transdermal devices. No criticality has been shown in using estrogen in combination with huperzine in improving cognitive function.

Accordingly, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal drug delivery device to deliver huperzine as disclosed by any of US '715, US '986 or CN '987, and include any of the permeation enhancers in the formulation as desired by any of the references, with reasonable expectation of success of the delivered transdermal patch in improving memory and cognitive function in patients in need.

3. Claims 1-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of US 6,352,715 ('715), US 6,159,986 ('986) or CN 1111987 ('987), in combination with US 6,019,988 ('988).

The teachings of US '715, US '986 and CN '987 are discussed above. The references, however, do not teach the specific permeation enhancers claimed by applicants, the blood plasma levels, or the estrogen in combination with huperzine.

US '988 teaches transdermal patches to deliver drugs such as acetylcholine esterase inhibitors comprising permeation enhancers selected from fatty acids, fatty alcohols, fatty acid esters, terpenes, surfactants, and pyrrolidone derivatives (col.19, line 15; col.20, lines 53-65).

It is within the skill in the art to adjust the amount of the drug in order to achieve a therapeutic blood level for a predetermined period.

Transdermal delivery of combination of drugs is known and widely used in the transdermal devices. No criticality has been shown in using estrogen in combination with huperzine in improving cognitive function.

Accordingly, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal drug delivery device to deliver huperzine as disclosed by any of US '715, US '986 or CN '987, and include any of the permeation enhancers in the formulation as desired by any of the references, motivated by the teaching of US '988 that the method and composition that increase the skin permeation of the drug increase the bioavailability of the drug into the systemic

circulation, col.5, lines 15-19, with reasonable expectation of success of the delivered transdermal patch in improving memory and cognitive function in patients in need.

Response to Arguments

4. Applicant's arguments filed 03/24/2003 have been fully considered but they are not persuasive.

Applicants' arguments:

- US '715 does not teach the use of penetration enhancer, however, co-solvents are seemingly suggested as possibly improving the penetration of the neutral forms of huperzine.
- US '986 teaches the herbal supplement for improving memory along with huperzine, but the herbal supplement is to be primarily formulated for oral delivery, and other forms as transdermal delivery are briefly mentioned.
- CN '987 teaches laurocapram and another agent as permeation enhancer.
- US '988 teaches a laundry list of drugs containing huperzine and a laundry list of enhancer.
- None of the cited references provide sufficient teaching or suggestion to be modified or combined in order to arrive at the present invention.
- The modification of combination of the references amount at most to allegation of hindsight reconstruction of the references.

Examiner's position:

- US '715 suggests the co-solvent that improves the penetration of huperzine, as applicants themselves admit. The rational to modify or to combine the prior art does not have to be expressly stated in the prior art; the rational may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art.
- US '986 clearly teaches the composition comprising huperzine and penetration enhancer, and co-administration of herbal extract, as applicants claim. The reference suggests the transdermal administration of the herbal extract. A conclusion of obviousness under 35 U.S.C. 103 (a) does not require absolute predictability, only a reasonable expectation of success; and references are evaluated by what they suggest to one versed in the art, rather than by their specific disclosure. *In re Bozek*, 163 USPQ 545 (CCPA 1969).
- CN '987 teaches clearly the transdermal huperzine and combination of penetration enhancers comprising laurocapram, which is a fatty acid derivative, and that reads on the applicants' claims.
- US '988 is relied upon for teaching the different kinds of penetration enhancers. A conclusion of obviousness under 35 U.S.C. 103 (a) does not require absolute predictability, only a reasonable expectation of success; and references are evaluated by what they suggest to one versed in the art, rather than by their specific disclosure. *In re Bozek*, 163 USPQ 545 (CCPA 1969).
- In response to applicant's argument that there is no suggestion to combine or modify the references, the examiner recognizes that obviousness can only be

established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal drug delivery device to deliver huperzine as disclosed by any of US '715, US '986 or CN '987, and include any of the permeation enhancers in the formulation as desired by any of the references, motivated by the teaching of US '988 that the method and composition that increase the skin permeation of the drug increase the bioavailability of the drug into the systemic circulation, col.5, lines 15-19, with reasonable expectation of success of the delivered transdermal patch in improving memory and cognitive function in patients in need.

- In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Conclusion

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US 5,663,344 disclosed a treating Alzheimer' disease using huperzine administered transdermally.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (703) 305-4048. The examiner can normally be reached on Monday through Thursday from 7:00 AM to 5:30 PM, Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.

Isis Ghali
Examiner
Art Unit 1615

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600